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<u>REMARKS</u>

Claims 26-43 are presently pending in the case.

Claim provisionally rejections under judicially created doctrine of Double Patenting

The Examiner provisionally rejected claims 31-34 and 39-43 under the judicially created doctrine of double patenting as being unpatentable over the claims of pending US Patent Application 10/245,705. Since the present case is otherwise in condition for allowance, the present case should be allowed to issue and the double patenting issue should be taken up in the pending application.

The Examiner also rejected claims 31-33 and 39-42 under the judicially created doctrine of double patenting as being unpatentable over claims 1-11 and 13-16 of US Patent 6,358,530. Claim 1 of US Patent 6,358,530 recites "a dispersibility-enhancing amount of a physiologically-acceptable, water-soluble polypeptide." Accordingly, the claims are distinct. In addition, the claims of 6,358,530 do not anticipate the present claims, as suggested by the Examiner. The claims of 6,358,530 do not recite, for example, the insulin composition of claims 31 and 39 or the amorphous particles recited in claim 39. Withdrawal of the rejection is requested.

History of parent application

This application is a continuation of co-pending U.S. Patent Application Serial No. 08/668,036, now US Patent 6,685,967. The presently pending claims are identical to the issued claims in 08/668,036 except that "in the range from 0.1 μ m to 5 μ m" has been replaced with "below 10 μ m".

US Patent Application 08/668,036 (now US Patent 6,685,967), the parent of the present case, was finally rejected by the Examiner. Applicant appealed the final rejections and the rejections were overturned by the Board of Patent Appeals and Interferences. The present claims are identical to the issued claims in 08/668,036 except that "in the range from $0.1~\mu m$ to $5~\mu m$ " has been replaced with "below $10~\mu m$ ", as stated above.

The below chart shows the present claims and the issued claims in the parent case and highlights the differences between the claims. The chart also shows the Examiner's rejections of the claims that were overturned by the Board.

| Currently pending claims (differences highlighted) | Issued claims in 08/668,036 (differences highlighted) | Rejection in 08/668,036 that was overturned by the Board of Patent Appeals and Interferences |
|--|---|---|
| 26. A method for | 15 (now 1). A method for | 35 USC 103(a) |
| preparing a stable, dry powder | preparing a stable, dry powder | Platz (5,354,562) and |
| insulin composition, said | insulin composition, said | AKZO (EP 0 360 340) |
| method comprising: | method comprising: | in view of |
| dissolving insulin in an | dissolving insulin in an | Manier (5,482,927) |
| aqueous buffer at a | aqueous buffer at a | Okada (4,211,769) |
| concentration in the range | concentration in the range | Hirai (4,659,696) |
| from 0.01% to 1% to form a | from 0.01% to 1% to form a | |
| solution; and | solution; and | l i |
| spray drying the | spray drying the | |
| solution to produce | solution to produce | · |
| substantially amorphous | substantially amorphous | · |
| particles having an average | particles having an average | J |
| size below 10 µm. | size in the range from 0.1 | · |
| | μm to 5 μm. | |
| 27. A method as in claim | 16 (2). A method as in claim | 35 USC 103(a) |
| 26, wherein the insulin is | 1, wherein the insulin is | Platz (5,354,562) and |
| dissolved in a aqueous buffer | dissolved in a aqueous buffer | AKZO (EP 0 360 340) |
| together with a pharmaceutical | together with a pharmaceutical | in view of |
| carrier, wherein a dry powder | carrier, wherein a dry powder | Manier (5,482,927) |
| having insulin present in | having insulin present in | Okada (4,211,769) |
| individual particles at from | individual particles at from | Hirai (4,659,696) |
| 5% to 99% by weight is | 5% to 99% by weight is | |
| produced upon spray drying. | produced upon spray drying. | |
| 28. A method as in claim | 17 (3). A method as in claim | 35 USC 103(a) |
| 27, wherein the | 2, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier is a | pharmaceutical carrier is a | AKZO (EP 0 360 340) |
| carbohydrate, organic salt, | carbohydrate, organic salt, | in view of |
| amino acid, peptide, or protein | amino acid, peptide, or protein | Manier (5,482,927) |
| which produces a powder | which produces a powder | Okada (4,211,769) |
| upon spray drying. | upon spray drying. | Hirai (4,659,696) |
| 29. A method as in claim | 18 (4). A method as in claim | 35 USC 103(a) |
| 28, wherein the | 3, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier is a | pharmaceutical carrier is a | AKZO (EP 0 360 340) |
| carbohydrate selected from the | carbohydrate selected from the | in view of |
| group consisting of mannitol, | group consisting of mannitol, | Manier (5,482,927) |
| raffinose, lactose, malto | raffinose, lactose, malto | Okada (4,211,769) |
| dextrin and trehalose. | dextrin and trehalose. | Hirai (4,659,696) |

| 00 | | |
|---------------------------------|--|--------------------------|
| 30. A method as in claim | 19 (5). A method as in claim | 35 USC 103(a) |
| 28, wherein the | 3, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier is an | pharmaceutical carrier is an | AKZO (EP 0 360 340) |
| organic salt selected from the | organic salt selected from the | in view of |
| group consisting of sodium | group consisting of sodium | Manier (5,482,927) |
| citrate, sodium acetate, and | citrate, sodium acetate, and | Okada (4,211,769) |
| sodium ascorbate. | sodium ascorbate. | Hirai (4,659,696) |
| | | Further in view of |
| | ' | Chien (5,042,975) and/or |
| | • | Markussen (4,946,828) |
| 31. An insulin composition | 20 (6). An insulin composition | 35 USC 103(a) |
| for pulmonary delivery, said | for pulmonary delivery, said | Platz (5,354,562) and |
| composition comprising a dry | composition comprising a dry | AKZO (EP 0 360 340) |
| powder of individual particles | powder of individual particles | in view of |
| which include insulin present | which include insulin present | Manier (5,482,927) |
| at from 20% to 80% by weight | at from 20% to 80% by weight | Okada (4,211,769) |
| in a pharmaceutical carrier | In a pharmaceutical carrier | Hirai (4,659,696) |
| material, wherein the particles | material, wherein the particles | (',,) |
| have an average size below 10 | have an average size in the | |
| μrö. | range from 0.1 μm to 5 μm. | |
| 32. An insulin composition | 21 (7). An insulin composition | 35 USC 103(a) |
| as in claim 31, wherein the | as in claim 6, wherein the | Platz (5,354,562) and |
| composition is substantially | composition is substantially | AKZO (EP 0 360 340) |
| free from penetration | free from penetration | in view of |
| enhancers. | enhancers. | Manier (5,482,927) |
| | | Okada (4,211,769) |
| · | | Hirai (4,659,696) |
| 33. An insulin composition | 22 (8). An insulin composition | 35 USC 103(a) |
| as in claim 31, wherein the | as in claim 6, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier | pharmaceutical carrier | AKZO (EP 0 360 340) |
| material comprises a | material comprises a | in view of |
| carbohydrate selected from the | carbohydrate selected from the | Manier (5,482,927) |
| group consisting of mannitol, | group consisting of mannitol, | Okada (4,211,769) |
| raffinose, lactose, malto | raffinose, lactose, malto | Hirai (4,659,696) |
| dextrin, and trehalose. | dextrin, and trehalose. | 1 III (4,007,070) |
| 34. An insulin composition | 23 (9). An insulin composition | 35 USC 103(a) |
| as in claim 31, wherein the | as in claim 6, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier | pharmaceutical carrier | AKZO (EP 0 360 340) |
| material comprises an organic | material comprises an organic | in view of |
| salt selected from the group | salt selected from the group | Manier (5,482,927) |
| consisting of sodium citrate, | consisting of sodium citrate, | Okada (4,211,769) |
| sodium gluconate, and sodium | sodium gluconate, and sodium | Hirai (4,659,696) |
| ascorbate. | ascorbate. | Further in view of |
| | and the factor of the factor o | Chien (5,042,975) and/or |
| | | |
| | | Markussen (4,946,828) |

| 35. A method for | 26 (10). A method for. | 35 USC 103(a) |
|--|--|-----------------------|
| preparing a stable, dry powder | preparing a stable, dry powder | Platz (5,354,562) and |
| insulin composition, said | insulin composition, said | AKZO (EP 0 360 340) |
| method comprising: | method comprising: | in view of |
| providing an aqueous | providing an aqueous | Manier (5,482,927) |
| solution of insulin and a | solution of insulin and a | Okada (4,211,769) |
| pharmaccutical carrier | pharmaceutical carrier | Hirai (4,659,696) |
| dissolved in an aqueous | dissolved in an aqueous | 1 |
| buffer, wherein the insulin is | buffer, wherein the insulin is | |
| present at 0.01% to 1% by | present at 0.01% to 1% by | |
| weight and comprises from | weight and comprises from | |
| 20% to 80% of the total | 20% to 80% of the total | 1 |
| weight of insulin and | weight of insulin and | |
| pharmaceutical carrier in the | pharmaceutical carrier in the | |
| solution; and | solution; and | |
| spray drying the | spray drying the | 1 |
| solution to produce | solution to produce | |
| amorphous particles | amorphous particles | |
| comprising both the insulin | comprising both the insulin | |
| and the pharmaceutical carrier | and the pharmaceutical carrier | |
| having an average size below | having an average size in the | |
| 10 μm and a moisture content | range from 0.1 μm to 5 μm | |
| below 10%. | and a moisture content below | |
| | 10%. | |
| 36. A method as in claim | 27 (11). A method as in claim | 35 USC 103(a) |
| 35, wherein the | 10, wherein the | Platz (5,354,562) and |
| pharmaceutical carrier is a | pharmaceutical carrier is a | AKZO (EP 0 360 340) |
| carbohydrate, organic salt, | carbohydrate, organic salt, | in view of |
| amino acid, peptide, or protein | amino acid, peptide, or protein | Manier (5,482,927) |
| which produces a powder | which produces a powder | Okada (4,211,769) |
| upon spray drying. | upon spray drying. | Hirai (4,659,696) |
| 37. A method as in claim | 28 (12). A method as in claim | 35 USC 103(a) |
| 36, wherein the carbohydrate | 11, wherein the carbohydrate | Platz (5,354,562) and |
| carrier is selected from the | carrier is selected from the | AKZO (EP 0 360 340) |
| group consisting of mannitol, | group consisting of mannitol, | in view of |
| raffinose, lactose, malto dextrin and trehalose. | raffinose, lactose, malto | Manier (5,482,927) |
| desarin and trenatose. | dextrin and trehalose. | Okada (4,211,769) |
| 38. A method as in claim | 20 (12) A mostle of an in all | Hirai (4,659,696) |
| | 29 (13). A method as in claim | 35 USC 103(a) |
| 36, wherein the carrier is an organic salt selected from the | 11, wherein the carrier is an | Platz (5,354,562) and |
| group consisting of sodium | organic salt selected from the | AKZO (EP 0 360 340) |
| citrate, sodium acetate, and | group consisting of sodium | in view of |
| sodium ascorbate. | citrate, sodium acetate, and sodium ascorbate. | Manier (5,482,927) |
| Sociulit ascordate. | Sodium ascordate. | Okada (4,211,769) |
| L | | Hirai (4,659,696) |

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|--------------------------------|--------------------------------|---|
| 39. (Previously presented) | 30 (14). An insulin | 35 USC 103(a) |
| An insulin composition for | composition for pulmonary | Platz (5,354,562) and |
| pulmonary delivery, said | delivery, said composition | AKZO (EP 0 360 340) |
| composition comprising: | comprising: | in view of |
| a dry powder of | a dry powder of | Manier (5,482,927) |
| individual amorphous particles | individual amorphous particles | Okada (4,211,769) |
| including both insulin and a | including both insulin and a | Hirai (4,659,696) |
| pharmaceutical carrier, | pharmaceutical carrier, | * |
| wherein the particles comprise | wherein the particles comprise | |
| from 20% to 80% insulin by | from 20% to 80% insulin by | · |
| weight, have an average | weight, have an average | |
| particle size below 10 µm, and | particle size in the range | |
| have a moisture content below | from 0.1 µm to 5 µm, and | |
| 10%. | have a moisture content below | |
| | 10%. | |
| 40. An insulin | 31 (15). An insulin | 35 USC 103(a) |
| composition as in claim 39. | composition as in claim 14, | Platz (5,354,562) and |
| wherein the particles consist | wherein the particles consist | AKZO (EP 0 360 340) |
| essentially of the insulin and | essentially of the insulin and | in view of |
| the pharmaceutical carrier. | the pharmaceutical carrier. | Manier (5,482,927) |
| mo parameter constant. | ino pharmaceutical carrier. | Okada (4,211,769) |
| | · | Hirai (4,659,696) |
| 41. An insulin | 32 (16). An insulin | 35 USC 103(a) |
| composition as in claim 39, | composition as in claim 14, | |
| wherein the composition is | wherein the composition is | Platz (5,354,562) and |
| substantially free from | substantially free from | AKZO (EP 0 360 340) in view of |
| penetration enhancers. | penetration enhancers. | |
| penenanon cimancers. | penedation engancers. | Manier (5,482,927) |
| | | Okada (4,211,769) |
| 42. An insulin | 22 (12) | Hirai (4,659,696) |
| | 33 (17). An insulin | 35 USC 103(a) |
| composition as in claim 39, | composition as in claim 14, | Platz (5,354,562) and |
| wherein the pharmaceutical | wherein the pharmaceutical | AKZO (EP 0 360 340) |
| carrier material comprises a | carrier material comprises a | in view of |
| carbohydrate selected from the | carbohydrate selected from the | Manier (5,482,927) |
| group consisting of mannitol, | group consisting of mannitol, | Okada (4,211,769) |
| raffinose, lactose, malto | raffinose, lactose, malto | Hirai (4,659,696) |
| dextrin, and trebalose. | dextrin, and trehalose. | |
| 43. An insulin composition | 34 (18). An insulin | 35 USC 103(a) |
| as in claim 39, wherein the | composition as in claim 14, | Platz (5,354,562) and |
| pharmaceutical carrier | wherein the pharmaceutical | AKZO (EP 0 360 340) |
| material comprises an organic | carrier material comprises an | in view of |
| salt selected from the group | organic salt selected from the | Manier (5,482,927) |
| consisting of sodium citrate, | group consisting of sodium | Okada (4,211,769) |
| sodium gluconate, and sodium | citrate, sodium gluconate, and | Hirai (4,659,696) |
| ascorbate. | sodium ascorbate. | Further in view of |
| | ľ | Chien (5,042,975) and/or |
| | | Markussen (4,946,828) |

A copy of the Board's decision has been included with the response of April 21, 2005 for the Examiner's convenience.

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Current rejections

The Examiner rejected claims 31-34 and 39-43 under 35 USC 103(a) as being obvious over Platz (5,354,562) alone or in combination with one or more of Chien (US 5,042,975), Markussen (US 4,946,828), Hansen (4,614,730), JP 56 138 110, or JP 56 138 111. The rejections are not believed to be proper in view of the Board of Patent Appeals and Interferences decision discussed above.

Conclusion

The Examiner is respectfully requested to consider the presently pending claims. Should the Examiner have any questions, the Examiner is requested to call the undersigned at the number given below.

Respectfully submitted,

NEKTAR THERAPEUTICS (formerly INHALE THERAPEUTIC SYSTEMS)

Dated: 15 FEB 2007

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